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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/657,516	09/08/2003	Francois Binette	022956-0225	7793

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EXAMINER	
QIAN, CELINE X	
ART UNIT	**PAPER NUMBER**
1636	

NOTIFICATION DATE	DELIVERY MODE
10/10/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

docket@nutter.com

Office Action Summary	Application No.	Applicant(s)	
	10/657,516	BINETTE ET AL.	
	Examiner	Art Unit	
	Celine X. Qian Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25-59* is/are pending in the application.

4a) Of the above claim(s) *25-47* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *48-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 25-59 are pending in the application. Claims 25-47 are withdrawn from consideration for being directed to non-elected subject matter. Claims 48-59 are pending in the application.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7/11/2007 has been entered.

Response to Amendment

All rejections applied to claims 1-4, 6-24 are moot in view of the cancellation.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 48-51, 54-56 are rejected under 35 U.S.C. 102(b)/(e) as being anticipated by Glorioso et al (US 6,413,511, IDS).

The claims are drawn to a genetically altered chrondrocyte that is used to express a therapeutic agent, and is effective to be delivered to a cell associated with a disorder and expresses a therapeutic agent to modify an environment surrounding the cell such that the chondrocyte is not structurally functional in the environment surrounding the cell.

Glorioso et al. disclose a chondrocyte that encodes a polypeptide of interest including interleukins, cytokines, tumor necrosis factors and biologically effective fragments thereof, which can be delivered to articular cartilage (see col. 27, lines 59-65, col. 21, lines 10-37). Glorioso also disclose that said chrondrocyte can be delivered with a gel matrix substrate to the damaged tissue site (see 29, lines 13-16). Glorioso further disclose that delivering a therapeutic agent to the damaged joint to treat arthritis (which can be an autoimmune disorder, see col. 27, lines 35-65). A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In the instant case, the intended use of the chrondrocyte does not impart a structural difference with what's disclosed in the prior art. Therefore, Glorioso et al. disclose the instantly claimed inventions.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 52 and 53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glorioso, in view of Bartholomew et al.

The teaching of Glorioso et al. is discussed above. However, Glorioso et al. do not teach a chrondrocyte produces an erythropoietin protein or an erythropoietin mimetibody.

Bartholomew et al. disclose human and baboon mesenchymal stem cells (MSC) that are genetically altered to express human EPO gene both *in vitro* and *in vivo* (see abstract). Bartholomew et al. also disclose that said MSC can differentiate into chondrocytes *in vivo*. Bartholomew et al. also teach that transduced bMSC are injected intramuscularly in NOD/SCID mice or implanted in either autologous or allogeneic baboon recipients, and wherein the human EPO was detected in the serum of both NOC/SCID mice and baboons.

It would have been obvious to one of ordinary skill in the art to express erythropoietin or erythropoietin mimetibody in the chrondrocyte taught by Glorioso et al. and combined with a biocompatible substrate based on the general knowledge in the art at the time of filing. The claimed invention would have been obvious because the substitution of one known element for another would have yielded predictable results to one of ordinary skill in the art. As evidenced

by the teaching of Glorioso et al., one of ordinary skill in the art would have reasonable expectation of success in introducing a transgene into chrondrocyte and express said protein *in vitro* or *in vivo*, and following the guidance of Bartholomew, one of ordinary skill in the art would have reasonable expectation of success in introducing the coding sequence of human EPO or mimetibody into a vector and express it *in vitro* or *in vivo*. Therefore, the invention would have been *prima facie* obvious to an ordinary artisan at the time the invention was made.

Claims 57-59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glorioso et al., in view of Okada et al (Biol. Pharm. Bull. 1997. Vol. 20, No.3, pages 255-258).

The teaching of Glorioso et al. is discussed above. However, Glorioso et al. do not teach a composition with a chrondrocyte with the gel matrix of an agarose, wherein the dimensions of the gel matrix determines the concentration of the chondrocytes within the gel matrix, and the concentration in the gel matrix is about 100,00 to 10 million cells per ml in a gel matrix volume of 0.05 to 10 ml.

Okada et al. teach microencapsulation of SK2 hybridoma cells in APA or agarose resulted in prolonged secretion of SK2mAb and improved effectiveness of the therapeutic treatment (see page 257, 2nd col). Okada et al. teach that the concentration of the APA-SK-2 cells is 5 million per ml of capsules and Aga-SK2 is $1.25X10^{7}$ per ml. Okada et al. also teach that the effectiveness of this cytomedicine has a limited duration because the number of viable cells decreases after 1-month post implantation. Okada et al. attribute the phenomena to the disappearance of inner space of the microcapsule for cell proliferation.

It would have been obvious to one of ordinary skill in the art to combine a biocompatible substrate such as agarose and the chrondrocyte taught by Glorioso et al. to form a drug delivery

system that is effective in prolonged delivery of the protein of interest based on the general knowledge in the art as demonstrated by Glorioso et al. and Okada et al. The claimed invention would have been obvious because the technique of microencapsulate cells with agarose is known to improve the effectiveness of biomedicine of using cells to deliver a protein of interest as demonstrated by Okada et al. Since Glorioso et al. teach delivering a therapeutic protein of interest using a chrondrocyte modified to express a therapeutic protein, it would have been obvious to one of ordinary skill in the art to encapsulate the cells in a biocompatible substrate such as agrose to predictably improve the function and effectiveness of the delivery. Since Okada et al. teach that the number of viable cells would decrease after a certain period of time due to the decreased space within the microcapsule, thus the duration of the medicine would be affected, it would have been obvious to one of ordinary skill in the art to use the dimension of the gel matrix to determine the concentration of the chondrocytes within the gel matrix such that it would have optimized result in achieving maximal survival of the chondrocytes and delivering of the therapeutic protein. The concentration taught by Okada et al. fall within the claimed range and determining the optimal concentration based on such teaching would have been routine experimentation to the ordinary artisan at the time the invention was made. Therefore, the claimed invention is obvious because a known technique is applied to a known composition to for improvement and yielded predictable results.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X. Qian Ph.D. whose telephone number is 571-272-0777. The examiner can normally be reached on 9:30-6:00 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joe Woitach Ph.D. can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Celine X Qian Ph.D.
Examiner
Art Unit 1636

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PRIMARY EXAM